

**REMARKS**

In the Official Office Action, Examiner:

- Rejected Claims 1, 3-6, 9-11, 13 and 14 under 35 U.S.C. §102(e) as being anticipated by Quake I (US 6,964,736);
- Rejected Claims 1, 3-6, 9-11, 13 and 14 under 35 U.S.C. §102(e) as being anticipated by Quake II (WO 99/61888);
- Rejected Claims 1-4, 7, 9, 11 and 13 under 35 U.S.C. §102(e) as being anticipated by Van den Berg (US 6,508,273);
- Rejected Claims 2 and 12 under 35 U.S.C. §103(a) as being obvious in view of Quake I and Schlenoff (US 6,841,054);
- Rejected Claims 2 and 12 under 35 U.S.C. §103(a) as being obvious in view of Quake II and Schlenoff;
- Rejected Claim 2 under 35 U.S.C. §103(a) as being obvious in view of Van den Berg and Schlenoff;
- Rejected Claims 5 and 10 under 35 U.S.C. §103(a) as being obvious in view of Van den Berg and Quake I; and,
- Rejected Claims 15 and 16 under 35 U.S.C. §103(a) as being obvious in view of Quake II and Troian (US 7,216,660) and Unno (US 7,024,281).

By this Reply, Claims 1, 6-8 and 11 are amended, and Claims 9 and 13-16 have been canceled. Therefore, upon entry of the amendments, Claims 1-8, 10, and 11 will remain at issue.

**Rejections under 35 U.S.C. §102(e)**

**The Van den Berg Reference**

Claims 1-4, 7, 9, 11 and 13 were rejected as being anticipated by U.S. Patent No. 6,508,273 ("Van den Berg"). Applicants respectfully submit that the claims as amended are novel over Van den Berg.

The amended claims are novel over Van den Berg because each claim includes a limitation directed to electrophoresis as the technique for driving the component flow. Van den Berg is directed to electroosmosis in which barrier layer charges created by an electrode (6) surrounding a channel (3) are traveling under the influence of a field (E) thereby creating bulk

flow due to drag between a boundary layer and the bulk (Van den Berg at columns 5 and 6). By contrast, the claims as amended require electrophoresis to drive the flow. With electrophoresis, it is the bulk charges which travel through a gel or capillary under the influence of an electric field.

Examiner argued that the electroosmosis apparatus of Van den Berg would be capable of electrophoresis. However, it appears unlikely that the electrodes (18) and (19) of Van den Berg could create the potential difference of Claim 1 for selecting a channel by virtue of the potential difference because the electrodes (18) and (19) are arranged to create surface charges in the channel as illustrated in Figures 1, 2a and 2b.

In any event, Van den Berg does not disclose voltage control means arranged such that the potential difference in a selected subsidiary channel is directed with an electrophoretic potential (or, in Van den Berg, the potential between electrodes (20) and (21/22)) and against it in any remaining channels. In fact, Van den Berg discloses the opposite as can be seen when considering Table 1 of Van den Berg. To select channel (15), the electrodes (17) and (18) are positive and the electrode (19) is negative. This is correct for electroosmotic flow based on the principles set out in Van den Berg, since the flow in the selected channel (15) has the same direction as the flow in the main channel (14) because the respective surface electrodes (17) and (18) have the same polarity resulting in barrier layer charges of the same polarity (see Figures 2a and b of Van den Berg). The flow in the remaining channel (16) is in the opposite direction due to the negative polarity of the electrode (19), as required to direct flow to channel (15). Accordingly, it can be seen that Van den Berg teaches that the remaining (and not the selected) channel has a local potential difference in the same direction as the overall driving field between electrodes (20) and (21/22). Therefore, Van den Berg discloses the exact opposite of what is claimed.

#### **The Quake References**

Claims 1, 3-6, 9-11, 13 and 14 were also rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 6,964,736 ("Quake I") and WO 99/61888 ("Quake II") (collectively "Quake"). Applicants respectfully submit the claims as amended are novel over Quake.

The claimed invention is novel over Quake I because, in contrast to Quake I, the molecules of the subject claims must be electrophoretically separated by an applied electrophoresis potential applied by a first voltage source and a switchable voltage control means to change the polarity of a potential difference by setting the polarity of the selected channel to be with the polarity of the electrophoresis potential driving overall flow. While Quake I describes the arrangement of Figure 4 as an "electrophoretic discrimination means," the overall flow is driven by positive pressure (see Quake I at column 7, lines 57 to 60; and at column 14, lines 1 to 3). Quake I thus cannot disclose the electrophoretic arrangement now claimed, let alone the specific approach for directing flow in an electrophoresis device of locally reversing the potential difference in non-selected channels with respect to the electrophoresis potential.

Quake II appears to be silent as to the specific means for driving overall flow in connection with the Figure 4a arrangement, and does not disclose the features claimed. To the contrary, it appears that the most plausible explanation is that Quake II also employs pressure driven flow as in Quake I. No consideration is given to the interaction between the local potential difference of the electrodes (112) and (114) and an electrophoresis potential driving overall flow. This is because Quake II does not disclose or even contemplate using this arrangement in an electrophoresis set-up.

Moreover, as is described on page 2 and pages 9 and 10 of the subject Application, the present invention addresses the problem of cross-contamination between the subsidiary channels. This is achieved by locally reversing electrophoretic flow at the junction in a non-selected subsidiary channel (due to the renewal potential difference). Quake teaches away from this notion and in fact teaches the exact opposite concept of maintaining flow in all subsidiary channels, the molecules being carried by a bulk solution stream due to pressure in Quake I (see Quake I at column 14, lines 1 to 20; see also Quake I at column 14, lines 35 to 38 and Quake II at page 65, line 17 to 22).

Furthermore, the claims are not obvious in view of Van den Berg and Quake. Van den Berg relies on a different principle of operation and teaches the exact opposite to what is claimed in terms of controlling the various electrodes. Quake also discloses a different, pressure driven system with no suggestion as to how this should be adapted for electrophoresis and teaches against a clean blocking of flows in the non-selected channels, which is the underlying idea of

the invention. Accordingly, neither Van den Berg nor Quake render the claimed invention obvious.

**Rejections under 35 U.S.C. §103(a)**

Regarding the dependent claims, these are novel and inventive by virtue of their dependency. Moreover, the prior art does not disclose the specific connection scheme of Claim 6 (use of two voltage sources), Claim 7 (shorting a point along the main channel to a point along the subsidiary channel using the intrinsic resistance of the channel to reverse the potential difference, as explained on pages 12 and 13 of the subject Application) and Claim 8, which has been acknowledged as allowable. Similar arguments as set out above apply to the method claims.

Regarding Claim 7, as explained above, Van den Berg is not relevant. Table 1 of Van den Berg merely discloses that the two electrodes can have the same polarity, and Van den Berg does not disclose two electrodes being shortened (i.e. at the same potential).

Claim 7 requires the electrophoresis potential applied over the main and a subsidiary channel which creates a continued voltage drop from one end of the device to the other due to the resistance of the channel. Thus, for example, the voltage will be high, for example, 10 in arbitrary units, at the bottom end (not shown) of the main channel below point B in Figure 3. B will be at a lower potential, for example, 6, and at A and C (without any shorting) at an even lower potential, for example, 4. The voltage at the branch point is intermediate these two voltages, for example, 5, and the top end of the channel will be at 0. Now, by shorting together a point in the main channel (B) with a point in a subsidiary channel (A), the local potential difference at the branch point will be  $5-4=1$  between the branch point and C and  $5-6=-1$  between the branch point and B, achieving the desired opposed potential differences as claimed without the need to switch high voltages. This is a significant advantage realized by Applicants' invention to achieve the reversal of potential by suitable shorting. Van Den Berg is of no relevance to this aspect of the invention. Therefore, Claim 7 is patentable over Van den Berg.

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**Conclusion**

In view of the amendments and foregoing traverse, Applicants respectfully request Examiner to reconsider the rejections, and allow the claims as amended. If deficiencies remain, Examiner may contact the undersigned to facilitate allowance of this case.

Respectfully submitted,

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